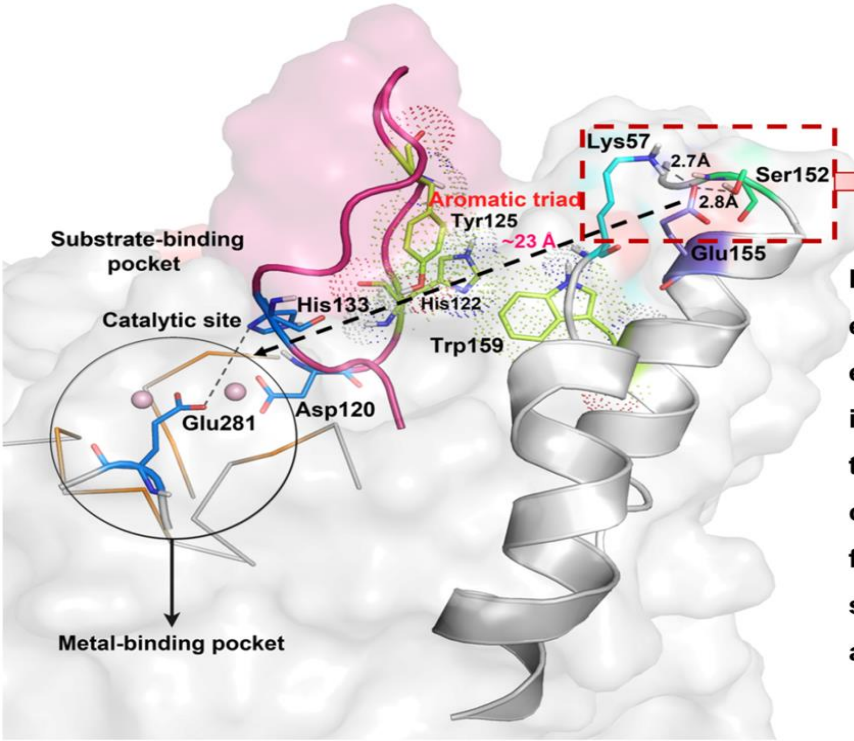
DBT-NII team gets new insight into pathogenesis of bacteria in human stomach

New Delhi, March 08: Helicobacter pylori arginase is important for pathogenesis of the bacterium in the human stomach. Despite conservation of the catalytic residues, this enzyme has a 13-residue insertion sequence in the middle of the protein sequence that is extremely crucial to function. This stretch is present only in the arginase of Helicobacter gastric pathogens, suggesting that this segment might have evolved in a unique manner to carry out a specific function.

In a new study, a team at DBT-National Institute of Immunology (DBT- NII), New Delhi used a combined approach to determine that Glu155 of this stretch interacts with both Lys57 and Ser152. These interactions are essential for positioning of the motif. The individual or double mutation of Lys57 and Ser152 to Ala considerably reduces catalytic activity with Lys57 to Ala being more significant, indicating these two residues are crucial to function.

The data suggest that the Lys57-Glu155-Ser152 interaction influences the positioning of the loop containing the catalytic His133 so that this His can participate in catalysis, thereby providing a mechanistic understanding into the role of this motif in catalytic function. Lys57 was also found only in the arginases of other Helicobacter gastric pathogens.

Based on the non-conserved motif, we found a structure-based new molecule, which specifically inhibits this enzyme. Thus, the present study not only provides a molecular basis into the role of this motif in function, but also offers an opportunity for the design of inhibitors with greater efficacy.



Dr. Sau and his team have elucidated the role of an evolutionary non-conserved motif in *Helicobacter pylori* arginase through positioning of the loop containing the catalytic residue for catalysis, and also identified a structure-based new inhibitor against this insertion sequence.

Dutta A, Sarkar D,..... & Sau AK (2021) Biochemical J (https://doi.org/10.1042/bcj20200978)

Reference:

Dutta A, Sarkar D, Murarka P, Kausar T, Narayan S, Mazumder M, Ainavarapu SRK, Gourinath S, Sau AK. An evolutionary non-conserved motif in Helicobacter pylori arginase mediates positioning of the loop containing the catalytic residue for catalysis. Biochem J. 2021 Jan 22:BCJ20200978. doi: 10.1042/BCJ20200978.

Contact Person & Contact Details: Dr. Apurba K. Sau; Email Id-apurba@nii.ac.in

Link: http://www.nii.res.in/content/national-institute-immunology